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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,145	09/21/2005	Anne T. Bruinvels	BJS-620-390	7778

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,145	BRUINVELS, ANNE T.	
	Examiner	Art Unit	
	Stacey MacFarlane	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-46 and 52* is/are pending in the application.

4a) Of the above claim(s) *29-31,33,36,39-41,43 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,28,32,34,35,37,38,42,44,45 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 3 and for condition of treatment applicant elects "negative symptoms of schizophrenia, for 5-HT2C receptor antagonist applicant elects deramciclane in the reply filed on June 20, 2007 is acknowledged. The traverse is on the ground(s) that the compounds of Table 3 are unified by having a relative affinity value of $\geq$ 1.80 as claimed. Applicant further traverses the species election on the basis that the conditions for treatment comprising schizophrenia, suicidality or cognitive impairment are not so distinct as to require an undue search burden. These arguments have been considered but are not found persuasive because the broadest claim (Claim 27) encompasses "a compound having a relative 5-HT2C affinity of $\geq$ 1.80" and thus encompasses the genus of compounds listed in Table 3. Applicant is reminded that if the generic claims are found to be allowable, all species would be examined. The compounds of Table 3 may have similar "relative affinity" or function but are not so linked in structure/function correlation to constitute a single genus of compounds. Applicant specifically requests that the elected compound deramciclane and its pharmacologically active metabolite, N-desmethyl-deramciclane be examined together. Examiner has found this to be persuasive as a search of the art for both encompass overlapping subject matter. However, the symptoms of schizophrenia, suicidality or mild cognitive impairment are not so linked as to be readily searched within the prior art. The claims are not drawn to methods of screening for compounds that have said affinity value but rather are drawn to methods for treatment

comprising administration of these compounds. Thus, if restriction were not required, the methods would require a search of the prior art for treatment comprising administration of each individual compound for the treatment of each condition claimed. Such a search would present an undue burden upon the examiner.

Thus, the requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-26 and 47-51 have been cancelled. Claims 29-31, 33, 36, 39-41, 43 and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 20, 2007.

3. Claims 27, 28, 32, 34, 35, 37, 38, 42, 44, 45 and 52, in so far as they read upon the elected species of negative symptoms of schizophrenia and deramciclane or N-desmethylderamciclane, will be considered upon their merits.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant claims the benefit of an earlier filing date to foreign application GB 0306604.0, filed March 21, 2003.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 32 and 42 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The compounds that are critical or essential to the practice of the method of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The incorporation of essential material in the claims by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f). Applicant is directed to Claims 32 and 42, and the supporting section of the specification, pages 29-30. See MPEP Section 608.01(p). Since the incorporation by reference is material to the claims, and there is no enabling description or explicit definition for this material in the disclosure, then the disclosure fails to meet the requirements of 35 U.S.C. 112.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 27, 28, 34, 35, 37, 38, 44, 45 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,589,996, filed March 16, 2001 and published December 6, 2001 ('996 Patent), and further in view of Meltzer HY, *The Role of Serotinin in Antipsychotic Drug Action*, Neuropyschopharmacology 21(2S): 106S-115S, August 1999.

These claims are drawn to a method for the treatment of a patient suffering from symptoms associated with a condition selected from the instantly elected negative symptoms of schizophrenia with a pharmaceutically effective amount of a compound having a relative 5-HT2C affinity of ≥ 1.80 with the proviso that the compound is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone (Claim 27). Dependent claims recite wherein the compound is the instantly elected deramciclane or N-desmethylderamciclane (Claim 52). Other dependent claims recite wherein the condition is refractory schizophrenia with the proviso that the compound is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone

(Claim 28); wherein the compound is the instantly-elected deramciclane or N-desmethylderamciclane (Claims 34 and 35). A method for the treatment of a patient suffering from symptoms associated with a condition of schizophrenia or refractory schizophrenia with a pharmaceutically effective amount of a 5-HT2C receptor antagonist with the proviso that the antagonist is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone (Claims 37 and 38); wherein the 5-HT2C receptor antagonist is the instantly-elected deramciclane or N-desmethylderamciclane (Claims 44 and 45).

The '996 Patent teaches administration to human patients an effective amount of deramciclane for the treatment of a disorder of the serotonergic system. The '996 Patent teaches deramciclane as an anti-anxiolytic and an antidepressant (Column 1 line 37 to Column 2 line 21). The '996 Patent teaches that deramciclane is an antagonist that specifically binds 5-HT2A and 5-HT2C receptors (Column 1, line 41). The '996 Patent further teaches that it is useful for the purpose of treating symptoms of anxiety disorders including, for example, persistent pathological anxiety, panic disorder and phobias and identifying restlessness, fatigue, difficulties in concentrating or mind going blank, irritability, muscle tension, and sleeping disturbances, as symptoms associated with anxiety and worry (Column 3, paragraph 3).

The '996 Patent does not specifically teach that the negative symptoms of schizophrenia or refractory schizophrenia as "serotonergic system disorders", however, the Meltzer reference teaches that serontonin receptors were well known in the art to

play a role in schizophrenia and in particular negative symptoms and refractory schizophrenia.

The Meltzer reference identifies 5-HT2A and 5-HT2C receptor antagonists as having "greater efficacy to reduce negative symptoms" of schizophrenia such as "affective flattening, anergia, anhedonia and avolition" (page 106S abstract and first paragraph), which one of ordinary skill in the art would recognize as equivalent to the negative symptoms listed in the instant specification, "flatness, poverty of speech and impaired executive functions" (page 1, lines 21-22). The reference states that such 5-HT antagonists as treatments for schizophrenic patients "who failed to respond to classical neuroleptic drugs" (*Id*), or schizophrenic patients who are considered "refractory" (page 109S, Column 1, last paragraph). Therefore, the Meltzer reference teaches that it was well known in the art, prior to the filing of the instant application, that the negative symptoms of schizophrenia and refractory schizophrenia were associated with disorder of the serotonergic system and that administering 5-HT2A and 5-HT2C receptor antagonists to a subject suffering therefrom can reduce those negative symptoms. Thus, the invention as a whole is *prima facie obvious*, if not actually anticipated by the methods as taught by the '996 Patent.

As stated on page 1 in the Applicant's Arguments/Remarks filed June 20, 2007, "The applicants submit that the presently disclosed invention is concerned with the identification of a new class of drugs that are particularly useful in the treatment of negative symptoms and cognitive deficits of schizophrenia and associated disorders. The drugs in this class all have a particular relative affinity for the 5HT2C receptor."

However, applicants claims are not drawn to methods of identification of a new class of drugs. The broadest Claim (Claim 27) is drawn to a method for the treatment of a patient suffering from symptoms associated with a condition, selected from the instantly elected negative symptoms of schizophrenia, with a pharmaceutically effective amount of a compound with the proviso that the compound is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone (Claim 27). This claim is interpreted as a method of treatment comprising the administration of a product-by-process. The clause that reads, "wherein the relative 5HT2C affinity is determined according to Formula 1:

Formula 1: $$\frac{X}{A} + \frac{X}{B} = Y$$

wherein X is the average affinity of a compound for interaction at the 5HT2C receptor and A and B are the average affinity values of a compound for interaction at two major sites other than the 5HT2C receptor" is interpreted as not limiting the scope of the claim by not affecting the structure of the compound. The court has stated that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." *Minton v. Nat'l Ass'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003). See MPEP § 2111.04. For examination purposes of the instant case, the method comprising the treatment of the same condition by the same product is considered art, regardless of the means by which the compound was determined to be useful for administration.

The discovery of an inherent property of a prior art process can not serve as a basis for patenting that process. See M.P.E.P. 2112.02 and *Ex parte Novitski*, 26

USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.).

Conclusion

4. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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